

CLAIMS

1. Drug-containing nanoparticles provided by causing primary nanoparticles containing a fat-soluble drug or a fat-solubilized water-soluble drug to act with a bivalent or trivalent metal salt.

2. Drug-containing nanoparticles provided by causing primary nanoparticles containing a fat-soluble drug or fat-solubilized water-soluble drug to act with a bivalent or trivalent metal salt to give secondary nanoparticles, and causing a monovalent to trivalent basic salt to act with the secondary nanoparticles.

3. The drug-containing nanoparticles according to claim 1 or 2, wherein the primary nanoparticles are produced by causing the fat-soluble drug or the fat-solubilized water-soluble drug, a medium- or long-chain organic compound having a negative ion residue and a surfactant to act with each other.

4. The drug-containing nanoparticles according to claim 3, wherein the medium- or long-chain organic compound having a negative ion residue is a C₆-C₂₄ fatty acid or its salt.

5. The drug-containing nanoparticles according to claim 4, wherein the C₆-C₂₄ fatty acid is selected from unsaturated fatty acids such as oleic acid, linoleic acid, and linolenic acid, and saturated fatty acids such as lauric acid, myristic acid, and palmitic acid.

6. The drug-containing nanoparticles according to claim 1 or 2, wherein the bivalent or trivalent metal salt is a calcium salt, a zinc salt, an iron salt, or a copper salt.

7. The drug-containing nanoparticles according to claim 2, wherein the monovalent to trivalent basic salt is selected from hydrogen carbonates, hydrogen phosphates, carbonates, phosphates, oxalates, lactates, and urates.

8. The drug-containing nanoparticles according to claim 1 or 2, wherein fat-solubilization of water-soluble drug is carried out by contact between the water-soluble drug and the bivalent or

trivalent metal ion, contact between the water-soluble drug and an acidic or basic polysaccharide, or adjustment of pH or change in ion strength of the solution in which the water-soluble drug is dissolved.

5 9. The drug-containing nanoparticles according to claim 8, wherein the bivalent or trivalent metal ion to be brought into contact with the water-soluble drug is selected from a zinc ion, a calcium ion, an iron ion, and a copper ion.

10 10. The drug-containing nanoparticles according to claim 3 or 9, wherein the surfactant is one or more selected from glycerin, lecithin, polyoxyethylene (20) sorbitan monooleate (Tween 80), polyoxyethylene (20) sorbitan monolaurate (Tween 20), polyoxyethylene (20) sorbitan monostearate (Tween 60), polyoxyethylene (20) sorbitan monoparmitate (Tween 40),
15 polyoxyethylene (20) sorbitan trioleate (Tween 85), polyoxyethylene (8) octylphenyl ether, polyoxyethylene (20) cholesterol ester, lipid-polyethylene glycol, polyoxyethylene hydrogenated castor oil, and fatty acid-polyethylene glycol copolymer.

20 11. The drug-containing nanoparticles according to any one of claims 1 to 10, wherein the fat-soluble drug or water-soluble drug is a chemical compound that has a molecular weight of 1,000 or less, exhibits bioactivity and are applicable to human.

25 12. The drug-containing nanoparticles according to claim 11, wherein the fat-soluble drug is insoluble to poorly soluble to water and soluble to organic solvents.

30 13. The drug-containing nanoparticles according to claim 11 or 12, wherein the fat-soluble drug is selected from steroid hormones, immuno suppressing or modulating agents, anticancer agents, antibiotics, chemotherapeutic agents, antiviral agents, non-steroidal anti-inflammatory agents, antipsychotic agents, calcium antagonists, antihypertensive agents, prostaglandin drugs, and lipophilic vitamins.

14. The drug-containing nanoparticles according to any one

of claims 11 to 13, wherein the fat-soluble drug is selected from testosterone enanthate, testosterone propionate, testosterone, estradiol, estradiol valerate, estradiol benzoate, dexamethasone acetate, betamethasone, betamethasone dipropionate, betamethasone valerate, prednisolone acetate, cyclosporine, tacrolimus, paclitaxel, irinotecan hydrochloride, cisplatin, methotrexate, carmofur, tegafur, doxorubicin, clarithromycin, aztreonam, cefdinir, nalidixic acid, ofloxacin, norfloxacin, ketoprofen, flurbiprofen, flurbiprofen axetil, chlorpromazine, diazepam, nifedipine, nicardipine hydrochloride, amlodipine besilate, candesartan cilexetil, aciclovir, vidarabine, efavirenz, alprostadil, dinoprostone, ubidecarenone, vitamin A (retinol), vitamin D, vitamin E, and vitamin K.

15. The drug-containing nanoparticles according to claim 11, wherein the water-soluble drug is a drug that is fat-solubilized by binding with a bivalent or trivalent metal ion.

16. The drug-containing nanoparticles according to claim 11 or 15, wherein the water-soluble drug is selected from water-soluble steroid hormones, immuno suppressing or modulating agents, anticancer agents, antibiotics, chemotherapeutic agents, antiviral agents, non-steroidal anti-inflammatory agents, antipsychotic agents, antihypertensive agents, prostaglandin drugs, and vitamins.

17. The drug-containing nanoparticles according to claim 11, 15, or 16, wherein the water-soluble drug is selected from betamethasone phosphate, dexamethasone phosphate, prednisolone phosphate, prednisolone succinate, hydrocortisone succinate, vancomycin, vincristine, vinplatin chloramphenicol succinate, latamoxef, cefpirome, carumonam, clindamycin phosphate, and abacavir.

18. The drug-containing nanoparticles according to claim 11, wherein the fat-soluble drug is testosterone enanthate, cyclosporine, betamethasone valerate, ubidecarenone, or vitamin A (retinol), and the water-soluble drug is betamethasone phosphate.

19. The drug-containing nanoparticles according to any one of claims 1 to 18, wherein the particles have a diameter ranging

from 1 to 200 nm.

20. A transdermal or transmucous external preparation comprising the drug-containing nanoparticles according to any one of claims 1 to 19.

5 21. The external preparation according to claim 20, wherein the external preparation is selected from ointments, gels, sublingual tablets, buccal tablets, liquids and solutions, sprays for buccal/lower respiratory tract, inhalations, suspensions, hydrogels, lotions, cataplasms, and patches.

10 22. An injectable preparation comprising the drug-containing nanoparticles according to any one of claims 1 to 19.

23. A process of producing drug-containing nanoparticles comprising; dissolving a fat-soluble drug or fat-solubilized water-soluble drug, a medium- or long-chain organic compound having a
15 negative ion residue, and a surfactant in an organic solvent or a water-containing organic solvent to give a solution; dispersing the solution in water to produce primary nanoparticles; and causing a bivalent or trivalent metal salt to act with the solution containing the primary nanoparticles.

20 24. A process of producing drug-containing nanoparticles comprising; dissolving a fat-soluble drug or fat-solubilized water-soluble drug, a medium- or long-chain organic compound having a negative ion residue and a surfactant in an organic solvent or a water-containing organic solvent to give a solution; dispersing the
25 solution in water to produce primary nanoparticles; causing a bivalent or trivalent metal salt to act with the solution containing the primary nanoparticles to produce secondary nanoparticles; and causing a monovalent to trivalent basic salt to act with the secondary nanoparticles.

30 25. The production process according to claim 23 or 24, wherein the organic solvent is one or more selected from acetone, ethanol, propanol, and butanol.

26. The production process according to claim 23 or 24,

wherein fat-solubilization of the water-soluble drug comprises bringing the water-soluble drug into contact with the bivalent or trivalent metal ion.